

Details of the Collaborative Activity

2020-21

Name of the Collaborating Institute: National Institute of Mental Health & Neurosciences (NIMHANS), Bengaluru.

Name of Collaborating Departments: Department of ENT, Yenepoya Medical College, Yenepoya Research Centre

Activities:

- **External training for ENT Post Graduates:**

Postgraduate students from Department of ENT, YMC have taken up External training of 15 days in the Department of Neurosurgery, NIMHANS

Details of Students

1. Dr. Rahul K,
2. Dr. Immelda Rani Thomas,
3. Dr. Maqbool MA,
4. Dr. Mohammed Jasim

- **Research Activities and joint publications**

Joint Research Projects:

1. Extramural funding: "Biomarker discovery in Sero-negative Neuromyelitis Optica (NMO)" Supported by ICMR - 2020-21: Co-PI. Dr. Keshavaprasad, YRC
2. Human Brain Proteome Map: Intramural support

Joint Publications:

- Santhosh Kumar R, Preethish-Kumar V, Mangalparthi KK, Unni S, Padmanabhan B, Prasad TSK, Nongthomba U, Atchayaram N, Narayanappa G. A Dominant C150Y Mutation in FHL1 Induces Structural Alterations in LIM2 Domain Causing Protein Aggregation In Human and Drosophila Indirect Flight Muscles. *Journal of Molecular Neuroscience*. 2021; 71(11):2324-35.

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Tel: 26588204-26588662-26589620

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110 029

भारतीय आयुर्विज्ञान अनुसंधान परिषद
INDIAN COUNCIL OF MEDICAL RESEARCH

वी. रामलिंगस्वामी भवन, अन्सारी नगर, पोस्ट बॉक्स 4911, नई दिल्ली - 110 029
V. RAMALINGASWAMI BHAWAN, ANSARI NAGAR, POST BOX 4911, NEW DELHI - 110 029

F. No. 33/16/2019-TF/Rare/BMS`

Date: 18.12.2020

Subject:- Payment of 1st and 2nd installment of the 1st year grant-in-aid for the project entitled "Biomarker discovery in seronegative Neuromyelitis Optica (NMO)"

Memorandum

The Director General of the Council sanctions the payment of Rs. 14,37,868/- [Rupees Fourteen Lakh Thirty Seven Thousand Eight Hundred Sixty Eight Only], as the 1st and 2nd installment of the 1st year grant for the period from 11.01.2021 to 10.01.2022 for incurring expenditure in connection with the above-mentioned project.

The amount of Rs. 14,37,868/- may be debited under the provision of made of on the above mentioned project for the year 2020-21.

A formal bill for Rs. 14,37,868/- is sent herewith for payment by cheque/demand draft for Rs. 14,37,868/- in favour of The Registrar, Center for Systems Biology and Molecular Medicine(CSBMM) Yenopoya Research center, Mangalore. This issued with the concurrence of the Finance Divn, vide RFC No. BMS/NTF/11/2020-21 Dated 16.12.2020

1. One JRF @ Rs. 31,000/- p.m + Rs 24 % HRA i.e. Rs. 7440/-	=	Rs. 461280/-
2. Non-recurring	=	Rs. 5,00,000/-
3. Consumables	=	Rs. 4,00,000/-
4. Contingencies	=	Rs. 25,000/-
5. Travel	=	Rs. 25,000/-
6. Overhead@3%	=	Rs. 26,588/-
Total Sanction	=	Rs. 14,37,868/-

Sr. Administrative Officer
For Director General

Accounts V. ICMR

Copy to:-

✓ The Registrar, Center for Systems Biology and Molecular Medicine (CSBMM) Yenopoya Research center, Yenopoya University, Mangalore- 575018

The grant has been sanctioned on the conditions laid down in out letter referred to above.

2 Dr. T.S. Keshava Prasad, Professor and Deputy Director, Center for Systems Biology and Molecular Medicine (CSBMM), Yenopoya Research Center, Yenopoya University, Mangalore-575018

It is requested that an audited statement of account together with utilization certificate of the grant received and utilized in _____ may kindly be sent to this office in due course.

3. IRIS Cell No. 2019-4687

Dr.Gangadhara Somayaji K.S.
Registrar
Yenopoya(Deemed to be University)
University Road, Deralakatte
Mangalore- 575 018, Karnataka

Sr. Administrative Officer
For Director General

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V. RAMALINGASWAMI BHAWAN, ANSARI NAGAR, POST BOX 4911, NEW DELHI - 110 029

No. 33/16/2019-TF/Rare/BMS

18.12.2020

To

The Registrar,
Center for Systems Biology and Molecular Medicine(CSBMM)
Yenepoya Research center, Yenepoya University
Mangalore- 575018

Subject:- Sanction of budget allotment for the new Research proposal entitled "*Biomarker discovery in seronegative Neuromyelitis Optica (NMO)*"

Sir/ Madam,

The Director General of the ICMR sanctions the above mentioned research scheme initially for the period of One Year from 11.01.2021 subject to extension up to the total duration specified in para 4 below:-

1. The Director General of the ICMR also sanctions the budget allotment of Rs.14,37,868/- as detailed in the attached statement for the period from 11.01.2021 to 10.01.2022 The grant-in-aid will be given subject to the following **Terms and conditions**.
2. The payment of the grant will be made in lump-sum to the Head of the Institute. The first installment of the grant will be paid generally as soon as report regarding appointment of the staff is received by the Council. The Staff appointed on the project should be paid as indicated in the budget statement.
3. The staff on the project will be recruited as per the rules and procedure of the host institute and second part of the undertaking be obtained from the employees of the project. The staff salary will be sanctioned/released only after submission of undertaking part-II (copy enclosed).
4. The demand for payment of the subsequent installment of the grant should be placed with the Council in the prescribed proforma. The approved duration of the scheme is **Three years**. The annual extension will be given only after review of the Annual Progress on the scheme during the previous year.
5. Five copies of the annual progress report in the attached prescribed proforma should be submitted to the Council every year after completion of ten months of the project giving complete actual details of the research work done. Failure to submit the report in time may lead to termination of project.
6. The Utilization Certificate & Statement of Expenditure must be send after completion of each one year duly signed by yours finance and account officers of your institute/university.
7. Receipt of this letter may please be acknowledged along with the acceptance of the Terms and Conditions within fort night.
8. The grant shall be utilized after following provision laid down in GFR and TA rules


Yours faithfully,

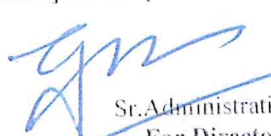
(G. S. Sandhu)
Sr. Administrative Officer
For Director General

Copy together with a copy of the budget statement forwarded to information to Dr. T.S. Keshava Prasad, Professor and Deputy Director, Center for Systems Biology and Molecular Medicine (CSBMM), Yenepoya Research Center, Yenepoya University, Mangalore-575018

2. Accounts. V for information.
3. Copy together with the budget forwarded to Budget Section [Finance Section] for compilation of the Council Budget
4. IRIS Cell No. 2019-4687

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Dr. Gangadhara Somayaji K.S.
Registrar
Yenepoya (Deemed to be University)
University Road, Derlakatte
Mangalore- 575 018, Karnataka


Sr. Administrative Officer
For Director General

BUDGET STATEMENT

2020-21

Subject: Research Project entitled "*Biomarker discovery in seronegative Neuromyelitis Optica (NMO)*" under Dr. T.S. Keshava Prasad, Professor and Deputy Director, Center for Systems Biology and Molecular Medicine (CSBMM), Yenepoya Research Center, Yenepoya University, Mangalore-575018

(11.01.2021 to 10.01.2022)

1. One JRF @ Rs. 31,000/- p.m + Rs 24 % HRA i.e. Rs. 7440/-	=	Rs. 461280/-
2. Non-recurring	=	Rs. 5,00,000/-
3. Consumables	=	Rs. 4,00,000/-
4. Contingencies	=	Rs. 25,000/-
5. Travel	=	Rs. 25,000/-
6. Overhead@3%	=	Rs. 26,588/-
Total Sanction	=	Rs. 14,37,868/-

Total budget allotment of Rs. 14,37,868/- [Rupees Fourteen Lakh Thirty Seven Thousand Eight Hundred Sixty Eight Only].


RFC No .BMS/NTF/11/2020-21 Dated 16.12.2020

No. 33/16/2019-TF/Rare/BMS

Received Contents


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A Dominant C150Y Mutation in *FHL1* Induces Structural Alterations in LIM2 Domain Causing Protein Aggregation In Human and *Drosophila* Indirect Flight Muscles

Rashmi Santhoshkumar¹ · Veeramani Preethish-Kumar² · Kiran K. Mangalaparathi³ · Sruthi Unni⁴ · Balasundaram Padmanabhan⁴ · Keshava Prasad T. S.⁵ · Upendra Nongthomba⁶ · Nalini Atchayaram² · Gayathri Narayanappa¹

Received: 25 June 2020 / Accepted: 11 December 2020

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Abstract

FHL1-related myopathies are rare X-linked dominant myopathies. Though clinically classified into several subgroups, spinal and scapuloperoneal muscle involvement are common to all. In this study, we identified c.449G > A, p.C150Y mutation by clinical exome sequencing in two patients from same family (son and mother) of Indian origin who presented with multiple contractures. Muscle biopsy showed numerous intracytoplasmic aggregates intensely stained on HE and MGT. The strong reactions to M-NBT revealed aggregates to be reducing bodies and positively labeled to anti-FHL1 antibody. Ultrastructurally, Z-band streaming and granular and granulo-filamentous material were seen. Further, the translational evidence of mutant peptide was confirmed using mass spectrometric analysis. To establish p.C150Y as the cause for protein aggregation, in vivo studies were carried out using transgenic *Drosophila* model which highlighted Z-band abnormalities and protein aggregates in indirect flight muscles with compromised physiological function. Thus, recapitulating the X-linked human disease phenotype. Additionally, the molecular dynamics simulation analysis unraveled the drastic change in α -helix of LIM2, the region immediately next to site of C150Y mutation that could be the plausible cause for protein aggregation. To the best of our knowledge, this is the first study of p.C150Y mutation in *FHL1* identified in Indian patients with in vivo and in silico analysis to establish the cause for protein aggregation in muscle.

Keywords FHL1 · Reducing body · Mutation · Mass spectrometry · Molecular dynamics simulation · *Drosophila melanogaster*

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Article

Extracellular Proteome Analysis Shows the Abundance of Histidine Kinase Sensor Protein, DNA Helicase, Putative Lipoprotein Containing Peptidase M75 Domain and Peptidase C39 Domain Protein in *Leptospira interrogans* Grown in EMJH Medium

Abhijit Sarma¹, Dhandapani Gunasekaran^{1,2}, Devasahayam Arokia Balaya Rex³, Thoduvayil Sikha^{1,4}, Homen Phukan¹, Kumar Mangalaparthy Kiran^{5,6}, Sneha M. Pinto^{3,5}, Thottethodi Subrahmanya Keshava Prasad^{3,5,6} and Madathiparambil G. Madanan^{1,*}



Citation: Sarma, A.; Gunasekaran, D.; Rex, D.A.B.; Sikha, T.; Phukan, H.; Kiran, K.M.; Pinto, S.M.; Prasad, T.S.K.; Madanan, M.G. Extracellular Proteome Analysis Shows the Abundance of Histidine Kinase Sensor Protein, DNA Helicase, Putative Lipoprotein Containing Peptidase M75 Domain and Peptidase C39 Domain Protein in *Leptospira interrogans* Grown in EMJH Medium. *Pathogens* **2021**, *10*, 852. <https://doi.org/>

Academic Editors: Sreekumari Rajeev and Alejandro Llanes

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Abstract: Leptospirosis is a re-emerging form of zoonosis that is caused by the spirochete pathogen *Leptospira*. Extracellular proteins play critical roles in the pathogenicity and survival of this pathogen in the host and environment. Extraction and analysis of extracellular proteins is a difficult task due to the abundance of enrichments like serum and bovine serum albumin in the culture medium, as is distinguishing them from the cellular proteins that may reach the analyte during extraction. In this study, extracellular proteins were separated as secretory proteins from the culture supernatant and surface proteins were separated during the washing of the cell pellet. The proteins identified were sorted based on the proportion of the cellular fractions and the extracellular fractions. The results showed the identification of 56 extracellular proteins, out of which 19 were exclusively extracellular. For those proteins, the difference in quantity with respect to their presence within the cell was found to be up to 1770-fold. Further, bioinformatics analysis elucidated characteristics and functions of the identified proteins. Orthologs of extracellular proteins in various *Leptospira* species were found to be closely related among different pathogenic forms. In addition to the identification of extracellular proteins, this study put forward a method for the extraction and identification of extracellular proteins.

Keywords: *Leptospira*; protein; extracellular; surface; secretory; pathogenic; proteomics

1. Introduction

Leptospirosis, the zoonotic disease once confined to posing a risk during agricultural activities, has been re-emerging due to increasing urbanization and slum areas that have increased the reservoir rodent population [1]. The increase in outbreaks during floods has been due to water getting contaminated with the urine from rats and several other domestic and wild animals that spread out during the floods. Humans exposed to such

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**COVID-19 Information**[Public health information \(CDC\)](#)[Research information \(NIH\)](#)[SARS-CoV-2 data \(NCBI\)](#)[Prevention and treatment information \(HHS\)](#)[Español](#)

FULL TEXT LINKS

[> OMICS](#). 2021 Sep;25(9):605-616. doi: 10.1089/omi.2021.0057. Epub 2021 Aug 24.

How to Achieve Therapeutic Response in Erlotinib-Resistant Head and Neck Squamous Cell Carcinoma? New Insights from Stable Isotope Labeling with Amino Acids in Cell Culture-Based Quantitative Tyrosine Phosphoproteomics

Ankit P Jain^{1 2}, Aneesha Radhakrishnan¹, Sneha Pinto^{1 3}, Krishna Patel^{1 4}, Manish Kumar^{1 5}, Vishalakshi Nanjappa¹, Remya Raja^{1 5}, Thottethodi Subrahmanya Keshava Prasad^{1 3 6}, Premendu P Mathur^{2 7}, David Sidransky⁸, Aditi Chatterjee^{1 5 3}, Harsha Gowda^{1 5 3}

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- 7 Department of Biochemistry & Molecular Biology, School of Life Sciences, Pondicherry University, Pondicherry, India.
- 8 Department of Otolaryngology-Head and Neck Surgery; Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.

PMID: 34432535 PMCID: PMC8591087 (available on 2022-09-01) DOI: [10.1089/omi.2021.0057](https://doi.org/10.1089/omi.2021.0057)**Abstract**

Resistance to cancer chemotherapy is a major global health burden. Epidermal growth factor receptor (*EGFR*) is a proven therapeutic target for multiple cancers of epithelial origin. Despite its overexpression in >90% of head and neck squamous cell carcinoma (HNSCC) patients, tyrosine kinase inhibitors such as erlotinib have shown a modest response in clinical trials. Cellular heterogeneity is thought to play an important role in HNSCC therapeutic resistance. Genomic alterations alone cannot explain all resistance mechanisms at play in a heterogeneous system. It is thus important to understand the biochemical mechanisms associated with drug resistance to determine potential strategies to achieve clinical response. We investigated tyrosine kinase signaling networks in erlotinib-resistant cells using quantitative tyrosine phosphoproteomics approach. We observed altered phosphorylation of proteins involved in cell adhesion and motility in erlotinib-resistant cells. Bioinformatics analysis revealed enrichment of pathways related to regulation of the actin

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cytoskeleton, extracellular matrix (ECM)-receptor interaction, and endothelial migration. Of importance, enrichment of the focal adhesion kinase (PTK2) signaling pathway downstream of *EGFR* was also observed in erlotinib-resistant cells. To the best of our knowledge, we present the first report of tyrosine phosphoproteome profiling in erlotinib-resistant HNSCC, with an eye to inform new ways to achieve clinical response. Our findings suggest that common signaling networks are at play in driving resistance to EGFR-targeted therapies in HNSCC and other cancers. Most notably, our data suggest that the PTK2 pathway genes may potentially play a significant role in determining clinical response to erlotinib in HNSCC tumors.

Keywords: cancer research; erlotinib resistance; focal adhesion kinase; head and neck cancer; quantitative tyrosine phosphoproteomics; tyrosine kinase inhibitors.

Related information

[MedGen](#)

LinkOut - more resources

Full Text Sources

[Atypon](#)

Research Materials

[NCI CPTC Antibody Characterization Program](#)

Miscellaneous

[NCI CPTAC Assay Portal](#)

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FULL TEXT LINKS



> [OMICS](#). 2021 Nov;25(11):693-710. doi: 10.1089/omi.2021.0158. Epub 2021 Oct 29.

The Normal Human Adult Hypothalamus Proteomic Landscape: Rise of Neuroproteomics in Biological Psychiatry and Systems Biology

Oishi Chatterjee^{1 2 3}, Lathika Gopalakrishnan^{1 3 4}, Praseeda Mol^{1 2}, Jayshree Advani¹, Bipin Nair², Susarla Krishna Shankar^{5 6}, Anita Mahadevan^{5 6}, Thottethodi Subrahmanya Keshava Prasad³

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PMID: 34714154 DOI: [10.1089/omi.2021.0158](https://doi.org/10.1089/omi.2021.0158)

Abstract

The human hypothalamus is central to the regulation of neuroendocrine and neurovegetative systems, as well as modulation of chronobiology and behavioral aspects in human health and disease. Surprisingly, a deep proteomic analysis of the normal human hypothalamic proteome has been missing for such an important organ so far. In this study, we delineated the human hypothalamus proteome using a high-resolution mass spectrometry approach which resulted in the identification of 5349 proteins, while a multiple post-translational modification (PTM) search identified 191 additional proteins, which were missed in the first search. A proteogenomic analysis resulted in the discovery of multiple novel protein-coding regions as we identified proteins from noncoding regions (pseudogenes) and proteins translated from short open reading frames that can be missed using the traditional pipeline of prediction of protein-coding genes as a part of genome annotation. We also identified several PTMs of hypothalamic proteins that may be required for normal hypothalamic functions. Moreover, we observed an enrichment of proteins pertaining to autophagy and adult neurogenesis in the proteome data. We believe that the hypothalamic proteome reported herein would help to decipher the molecular basis for the diverse range of physiological functions attributed to it, as well as its role in neurological and psychiatric diseases. Extensive proteomic profiling of the hypothalamic nuclei would further elaborate on the role and functional characterization of several

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FULL TEXT LINKS

[> J Cell Commun Signal](#). 2021 Nov 1. doi: 10.1007/s12079-021-00653-z. Online ahead of print.

Opioid receptors signaling network

Lathika Gopalakrishnan^{1 2 3}, Oishi Chatterjee^{1 3 4}, Namitha Ravishankar¹, Sneha Suresh¹, Rajesh Raju⁵, Anita Mahadevan^{6 7}, T S Keshava Prasad⁸

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- ⁶ Department of Neuropathology, National Institute of Mental Health and Neurosciences, Bangalore, 560 029, India.
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PMID: 34724150 DOI: [10.1007/s12079-021-00653-z](https://doi.org/10.1007/s12079-021-00653-z)

Abstract

Opioid receptors belong to the class A G-protein-coupled receptors and are activated by alkaloid opiates such as morphine, and endogenous ligands such as endorphins and enkephalins. Opioid receptors are widely distributed in the human body and are involved in numerous physiological processes through three major classical opioid receptor subtypes; the mu, delta and kappa along with a lesser characterized subtype, opioid receptor-like (ORL1). Opioids are the most potent analgesics and have been extensively used as a therapeutic drug for the treatment of pain and related disorders. Chronic administration of clinically used opioids is associated with adverse effects such as drug tolerance, addiction and constipation. Several investigations attempted to identify the molecular signaling networks associated with endogenous as well as synthetic opiates, however, there is a paucity of a cumulative depiction of these signaling events. Here, we report a systemic collection of downstream molecules pertaining to four subtypes of opioid receptors (MOR, KOR, DOR and ORL1) in the form of a signaling pathway map. We manually curated reactions induced by the activation of opioid receptors from the literature into five categories- molecular association, activation/inhibition, catalysis, transport, and gene regulation. This led to a dataset of 180 molecules, which is collectively represented in the opioid receptor signaling network following NetPath criteria. We believe that the public availability of an opioid receptor signaling pathway map can accelerate biomedical research in this area because of its high therapeutic significance. The opioid receptors signaling pathway map is

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